

Peer Review File

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Comment 1: The purpose of this article is not clear. The last two sentences of the Background and Objectives section of the abstract, “It is known that the data available so far are limited regarding the effect of post-mastectomy radiotherapy (PMRT) in PIBR. This all well true with data about the effect of previous radiotherapy/neoadjuvant radiotherapy (HR). Hence this review was undertaken,” do not clearly explain the purpose of the article. If the purpose of the article is to review the impact of pre-mastectomy and post-mastectomy radiation therapy on outcomes after prepectoral implant-based breast reconstruction, this should be stated in the Background and Objectives section.

Reply 1: This has been clarified in the manuscript.

Change in the text: “Hence this review was undertaken to study the effect of RT (both pre -and post- mastectomy) on PIBR.”

Comment 2: The fourth paragraph of the Discussion states, “Recently, the results of Sinnott et al. published results of their study. They addressed the impact of neoadjuvant RT on PIBR.” Although Sinnott et al. published an article describing the impact of pre-mastectomy versus post-mastectomy radiation therapy on outcomes in prepectoral implant-based breast reconstruction¹, this is not standard of care. The last sentence of the Conclusion section of the abstract, “Previous RT per se is not a contraindication to the procedure,” should not be a conclusion of the study because in most cases previous RT is a contraindication to implant-based breast reconstruction. Patients in the Sinnott et al study with pre-mastectomy radiation who underwent prepectoral implant-based breast reconstruction accepted the higher complication rate associated with this procedure and declined autologous reconstruction procedure.¹ Furthermore, the use of the “neoadjuvant” radiation therapy to describe the results of the Sinnott et al. study is incorrect, as explained below.

Reply 2: This was not a conclusion of Sinnott et al study . It is our narrative review conclusion based on different studies that we included. I have added “absolute contraindication “ to text to avoid confusion. We agree with Joint consensus that was published by Vidya R et al . Every patient with previous RT to be individualised and risk of complication to be discussed. Furthermore accepted by the patient. “Vidya R, Berna G, Sbitany H, et al. Prepectoral implant-based breast reconstruction: a joint consensus guide from UK, European and USA breast and plastic reconstructive surgeons. *Ecancermedicalscience*. 2019;7;13:927.”

Change in the text: “ Previous RT per se is not an absolute contraindication to the procedure”

Comment 3: In the last sentence of the abstract, “This all well true with data about effect of previous radiotherapy/neoadjuvant radiotherapy (RT),” the use of the word

“neoadjuvant radiotherapy” is incorrect. The patients in the Sinnott et al. study with premastectomy radiation who underwent prepectoral implant-based breast reconstruction did not have neoadjuvant radiation therapy.¹ These patients had a history of previous whole breast radiation years prior to mastectomy and prepectoral implant-based reconstruction for either DCIS or invasive cancer treated with breast conservation therapy and developed a recurrence or secondary cancer years later.¹ Neoadjuvant radiation therapy is radiation therapy that is administered prior to surgery. In breast cancer patients, neoadjuvant radiation is often administered in the case of inoperable locally advanced breast cancer for tumor downstaging and to enable surgical resection.

Reply 3: Mistake acknowledged. However it was mentioned in the abstract based on the joint consensus guide from UK, European and USA breast and plastic reconstructive surgeons (reference 3) – I have removed it to avoid any confusion.

Change in the text: The sentence was removed.

Comment 4: There is not a Results section of the Abstract.

Reply 4: According to narrative review checklist there is no results subsection in the Abstract. Results were included under Methods “19 studies reporting on impact of RT in PIBR or mentioned its effect met the inclusion criteria”

Change in the text: Results title was added next to methods.

Comment 5: The first sentence of the Conclusion section of the abstract, “PIBR proves to be a better technique in suitable non-irradiated patients compared to subpectoral placement,” is not an appropriate conclusion to be drawn from this study, as it was not an objective of the study. The authors did not perform this study to compare the efficacy of prepectoral versus subpectoral implant reconstruction in breast cancer patients. The authors should not report this as a conclusion of their study because it was reported as a conclusion of another study included in their review.²

Reply 5: Sentence was removed.

Change in text: Sentence was removed.

Comment 6: In the eighth paragraph of the Discussion, the authors state, “Sinnott et al. published a comparison of prepectoral and subpectoral procedures.² They found that subpectoral reconstruction showed higher capsular contracture rate than PIBR especially in irradiated breasts. They related that to the ability of ADM to prevent capsular contracture and the effectiveness of prepectoral implant approach.” First, the capsular contracture rate between prepectoral and subpectoral implant reconstruction patients without postmastectomy radiation therapy was not statistically significantly different, although it approached significance. Second, the Sinnott et al. authors did not attribute the increased capsular contracture rate in subpectoral implant-reconstruction with postmastectomy radiation to the ability of ADM to prevent capsular contracture. In the Sinnott et al study, both prepectoral and subpectoral implant-based breast reconstructions incorporated the use of ADM. This is explained in the first sentence of the second paragraph of the Results section of the

Sinnott et al. paper, “It is important to note that all the reconstructions in the both pre- and subpectoral groups were performed using porcine-derived ADM because it is believed that ADM may protect against capsular contracture after implant-based breast reconstruction in non-radiated and PMRT settings.”

Reply 6 : Comment on ADM was removed.

Change in the text: Comment removed.

Comment 7: Although the authors address an important topic in their review article that attempts to evaluate the impact of radiation therapy on prepectoral implant-based breast reconstruction, a topic of this importance requires a more comprehensive systematic review or meta-analysis.

Reply 7: We completely agree on the above comment. However this narrative review was chosen on at the time being until more comprehensive review is done.

Change in the text: None.